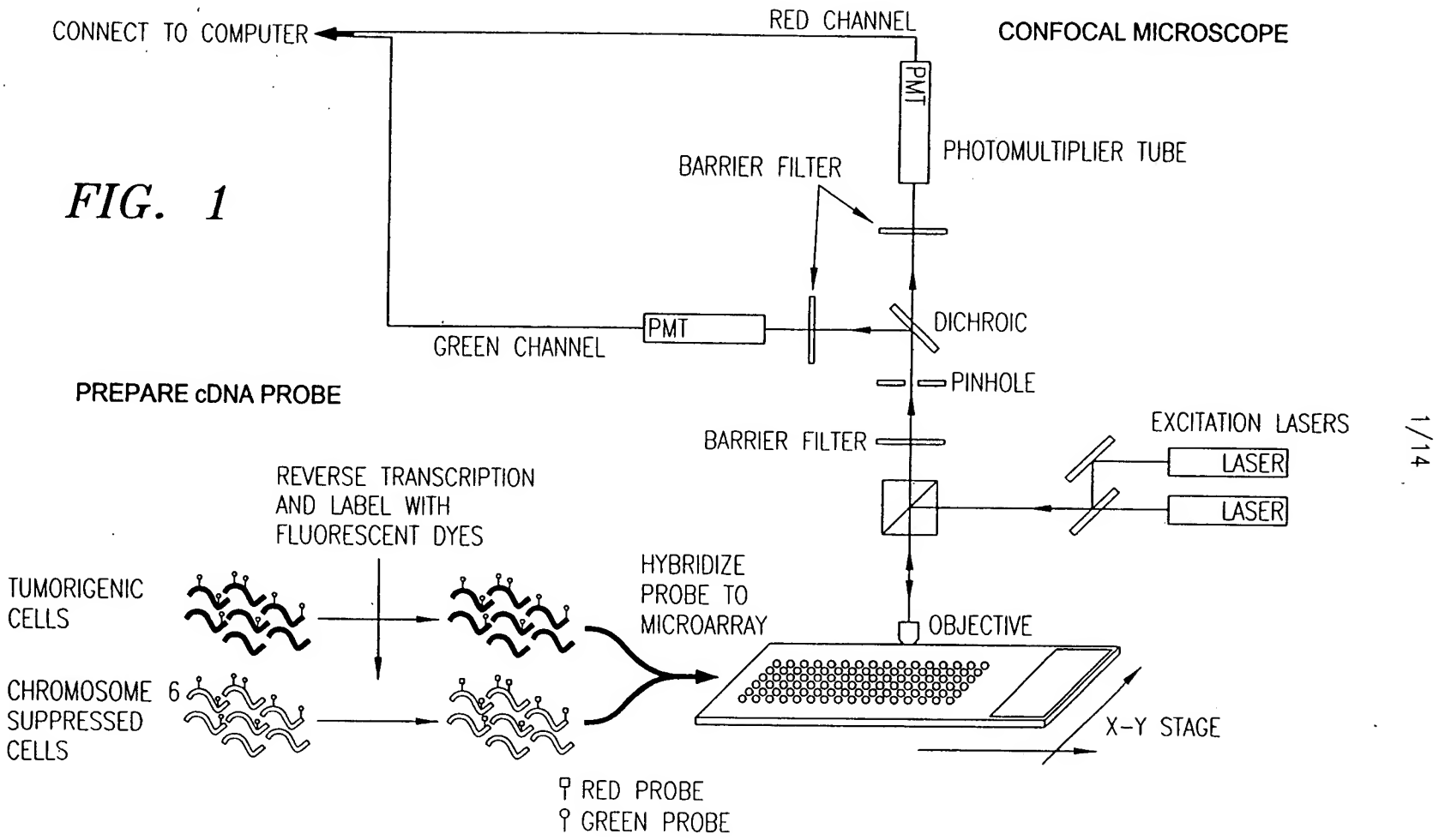

FIG. 1

1/14

BDI-01940.000

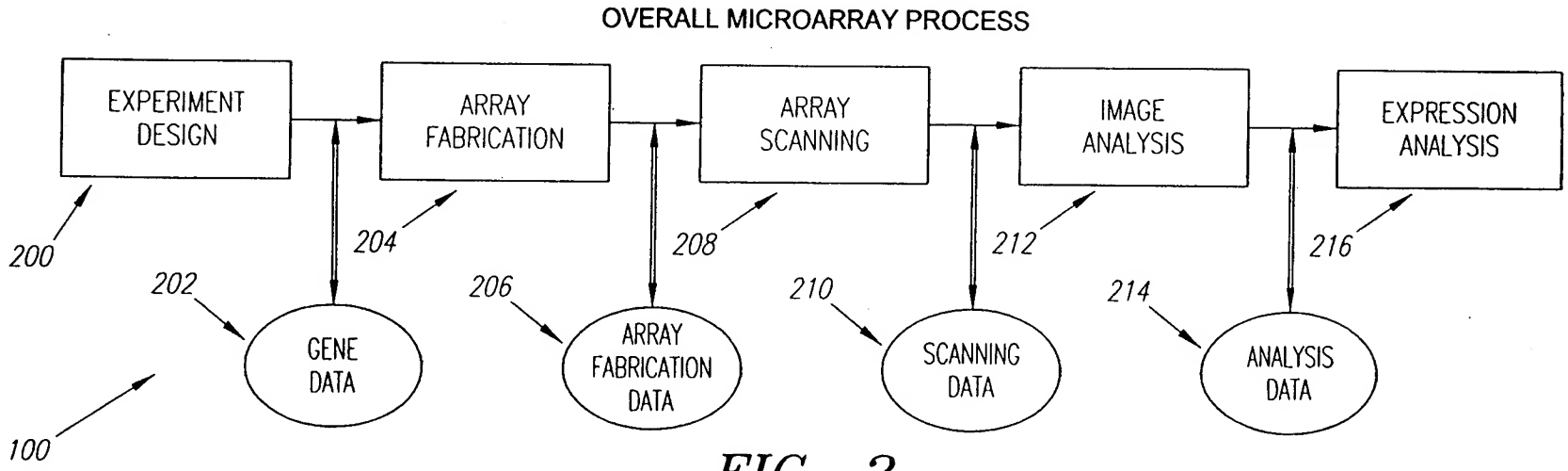
OVERALL MICROARRAY PROCESS
EXPERIMENT DESIGN
ARRAY FABRICATION
ARRAY SCANNING
IMAGE ANALYSIS
EXPRESSION ANALYSIS
200
204
208
212
216
202
206
210
214
GENE DATA
ARRAY FABRICATION DATA
SCANNING DATA
ANALYSIS DATA
100

FIG. 2

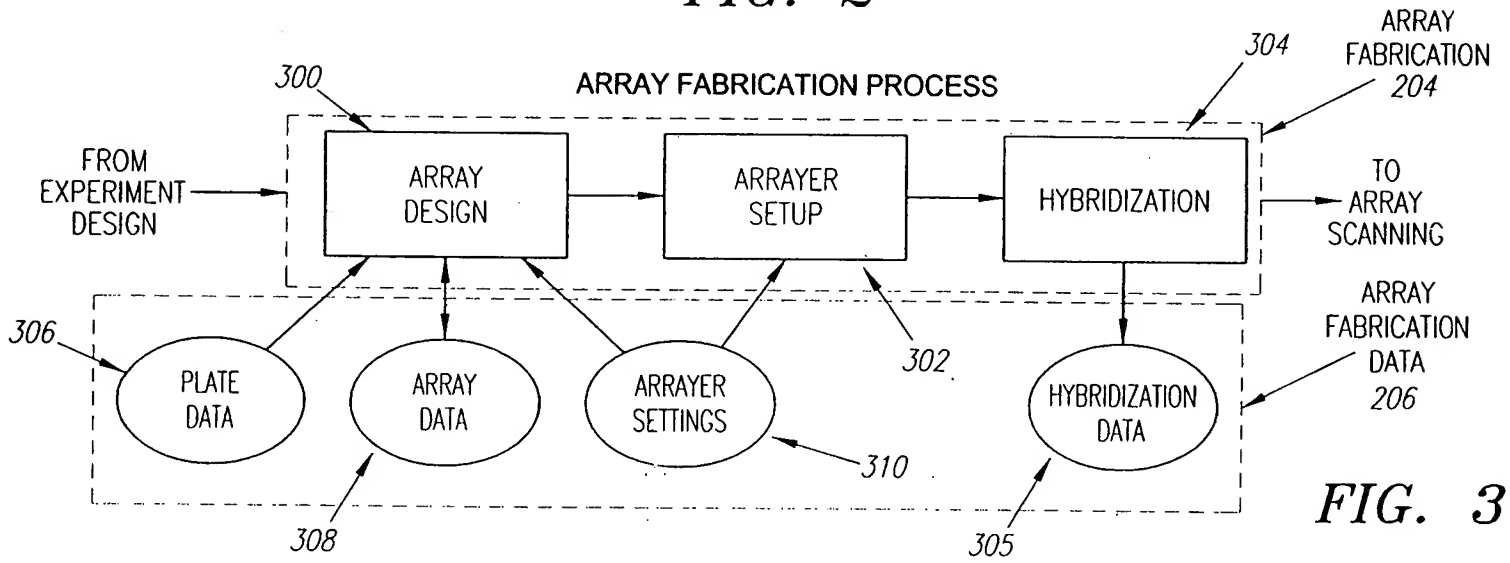
ARRAY FABRICATION PROCESS
300
304
ARRAY FABRICATION 204
FROM EXPERIMENT DESIGN
ARRAY DESIGN
ARRAYER SETUP
HYBRIDIZATION
TO ARRAY SCANNING
306
PLATE DATA
ARRAY DATA
ARRAYER SETTINGS
302
HYBRIDIZATION DATA
ARRAY FABRICATION DATA 206
310
308
305

FIG. 3

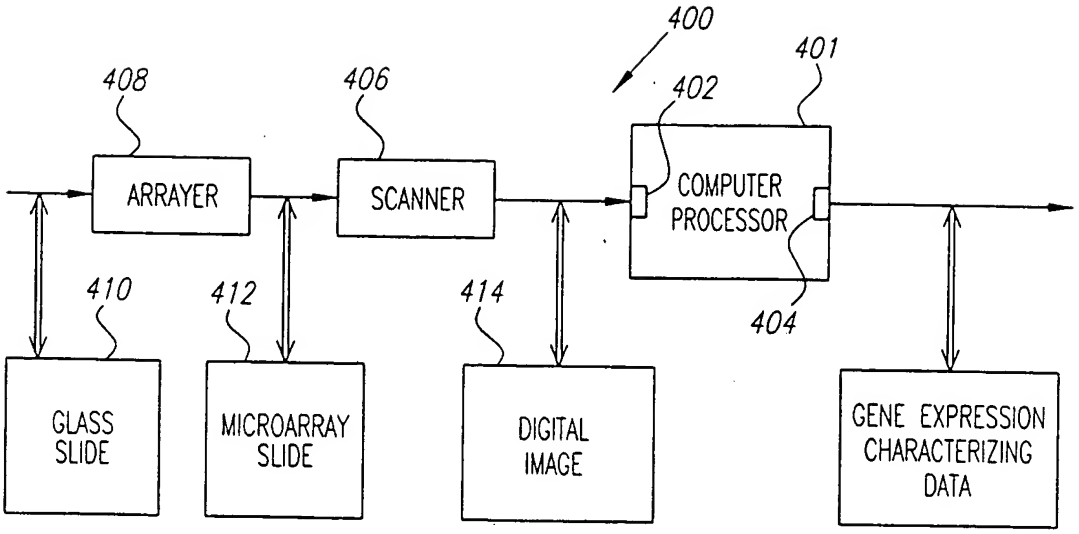
400
401
408
406
402
ARRAYER
SCANNER
COMPUTER PROCESSOR
410
412
414
404
GLASS SLIDE
MICROARRAY SLIDE
DIGITAL IMAGE
GENE EXPRESSION CHARACTERIZING DATA

FIG. 4

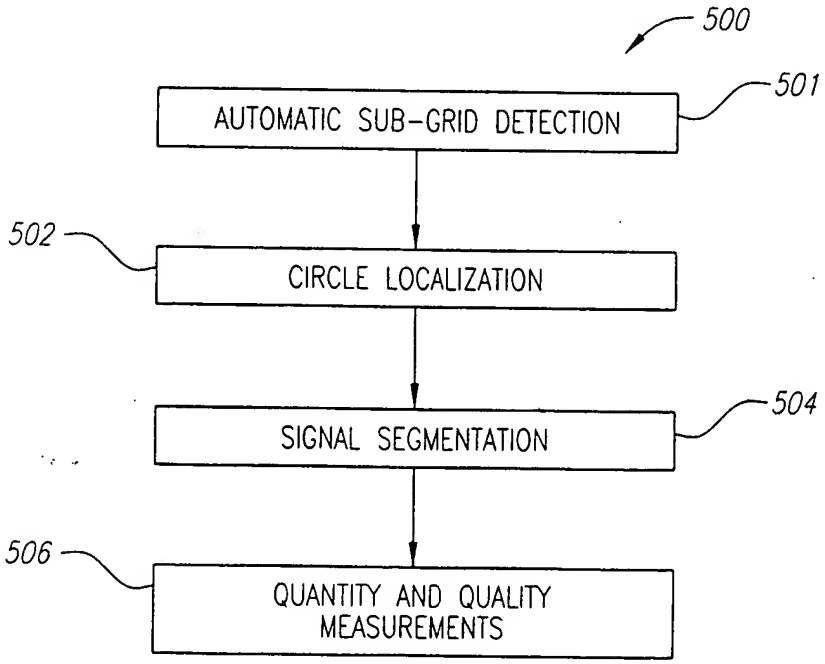
500
501
AUTOMATIC SUB-GRID DETECTION
502
CIRCLE LOCALIZATION
504
SIGNAL SEGMENTATION
506
QUANTITY AND QUALITY MEASUREMENTS

FIG. 5

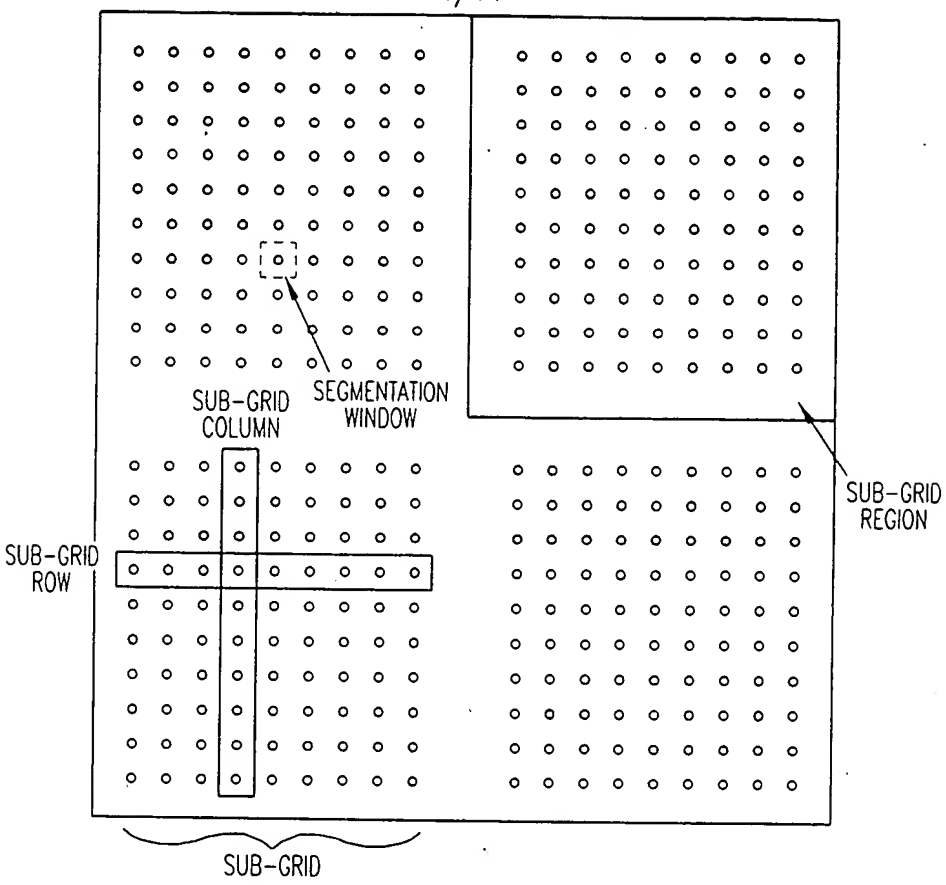
SUB-GRID COLUMN
SEGMENTATION WINDOW
SUB-GRID REGION
SUB-GRID ROW
SUB-GRID
2 x 2 MICROARRAY

FIG. 6

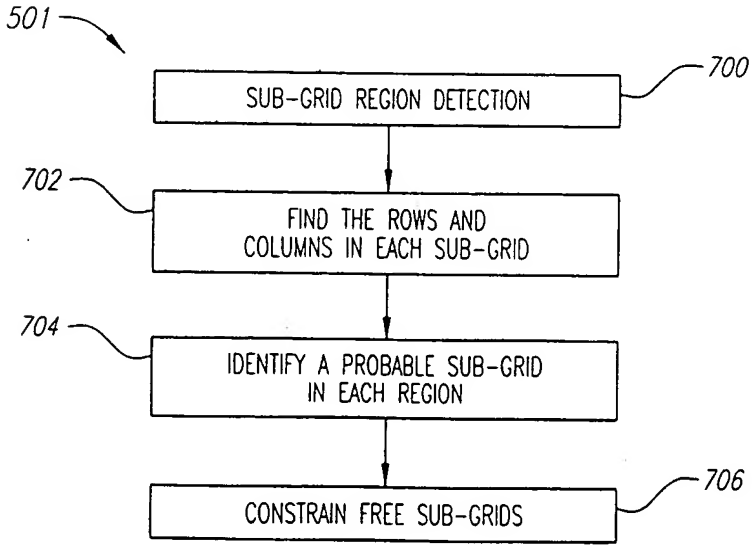
501
SUB-GRID REGION DETECTION
700
702
FIND THE ROWS AND COLUMNS IN EACH SUB-GRID
704
IDENTIFY A PROBABLE SUB-GRID IN EACH REGION
CONSTRAIN FREE SUB-GRIDS
706

FIG. 7

SUB-GRID REGION DETECTION

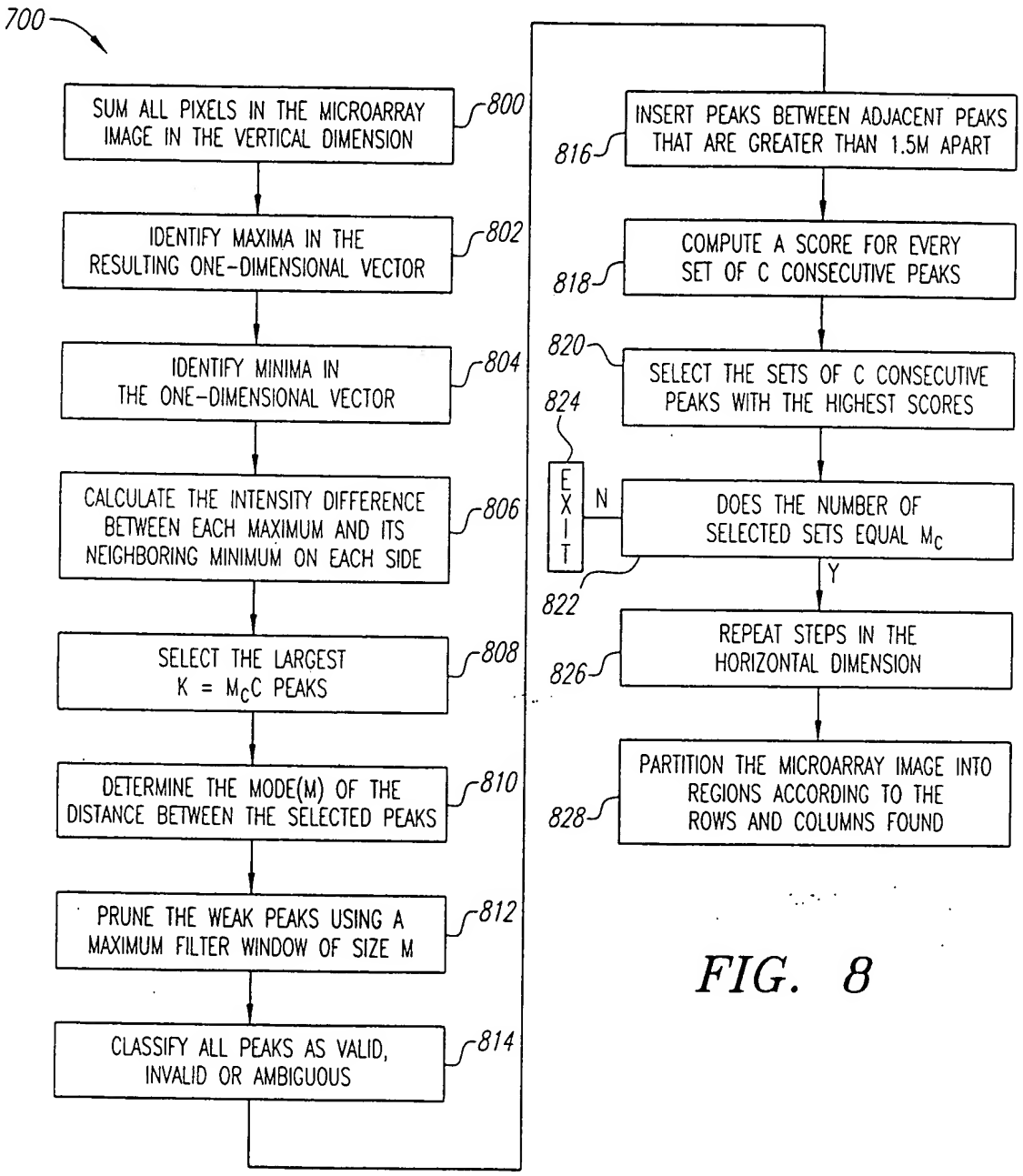

FIG. 8

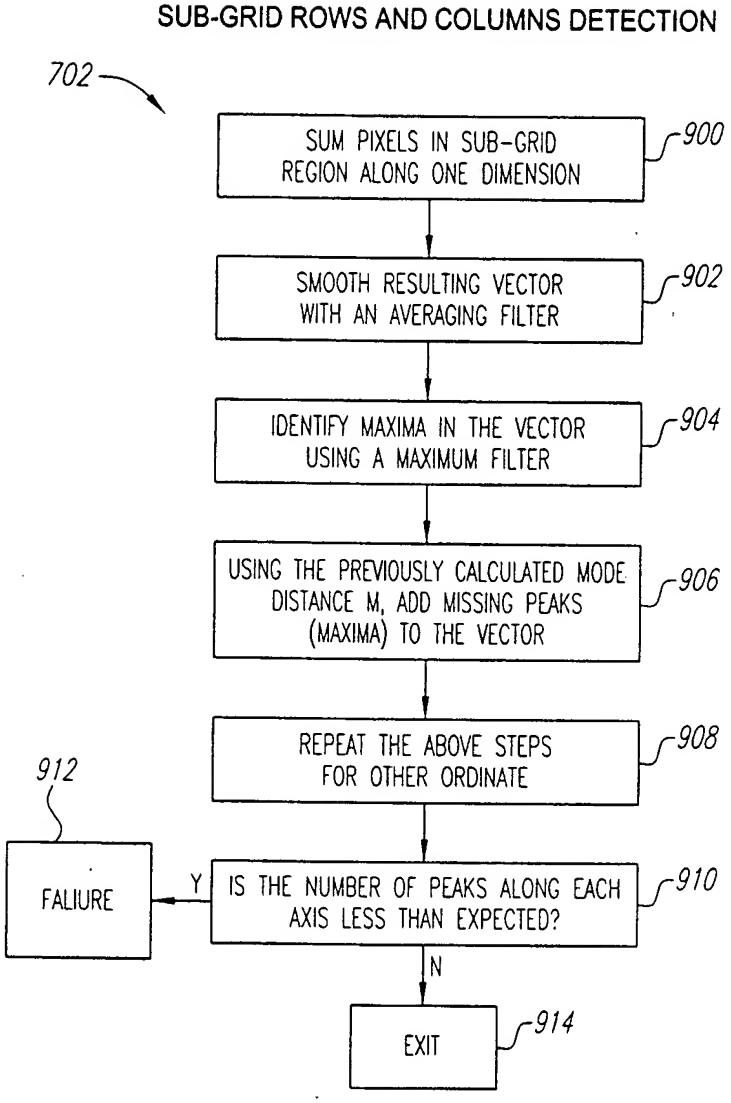
SUB-GRID ROWS AND COLUMNS DETECTION
702
SUM PIXELS IN SUB-GRID REGION ALONG ONE DIMENSION
900
SMOOTH RESULTING VECTOR WITH AN AVERAGING FILTER
902
IDENTIFY MAXIMA IN THE VECTOR USING A MAXIMUM FILTER
904
USING THE PREVIOUSLY CALCULATED MODE DISTANCE M, ADD MISSING PEAKS (MAXIMA) TO THE VECTOR
906
REPEAT THE ABOVE STEPS FOR OTHER ORDINATE
908
912
FALIURE
Y
IS THE NUMBER OF PEAKS ALONG EACH AXIS LESS THAN EXPECTED?
910
N
EXIT
914

FIG. 9

IDENTIFYING SUB-GRIDS IN EACH SUB-GRID REGION

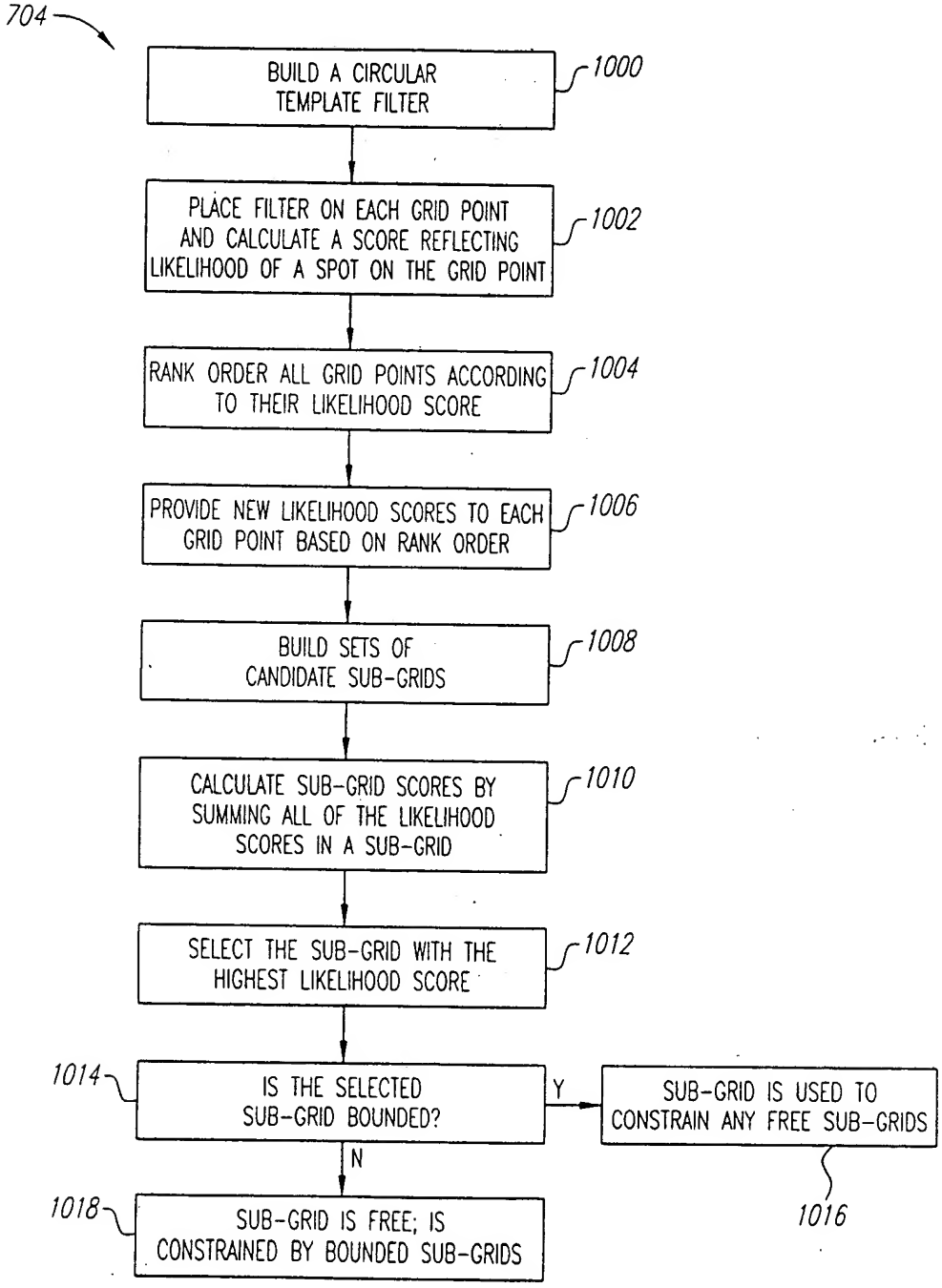

FIG. 10

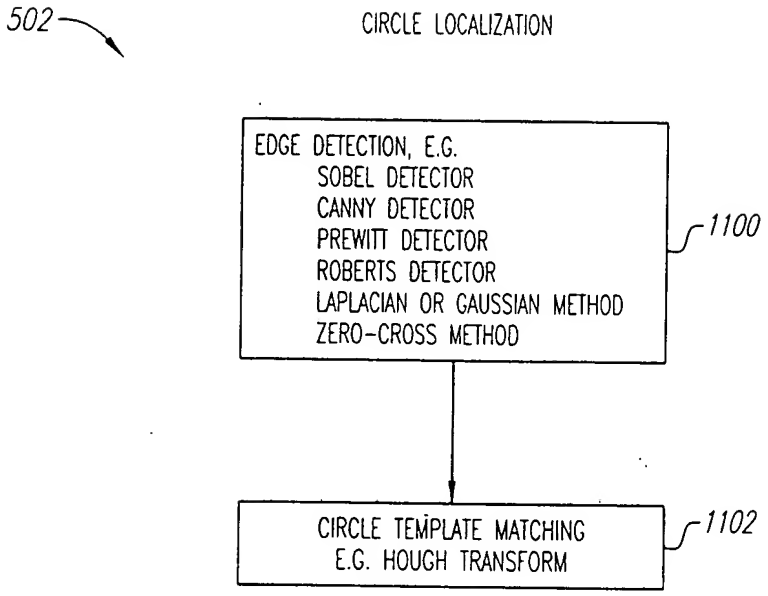
502
CIRCLE LOCALIZATION
EDGE DETECTION, E.G.
SOBEL DETECTOR
CANNY DETECTOR
PREWITT DETECTOR
ROBERTS DETECTOR
LAPLACIAN OR GAUSSIAN METHOD
ZERO-CROSS METHOD
1100
CIRCLE TEMPLATE MATCHING
E.G. HOUGH TRANSFORM
1102

FIG. 11

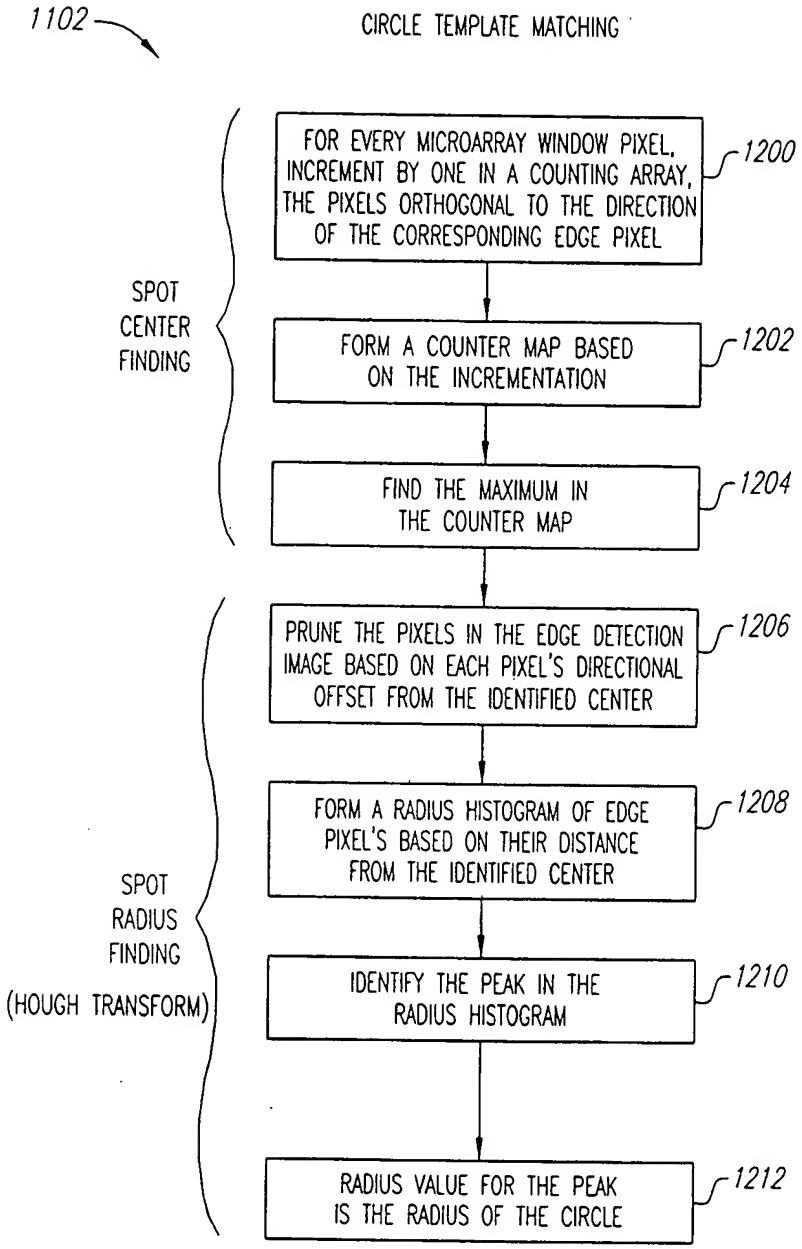
1102
CIRCLE TEMPLATE MATCHING
FOR EVERY MICROARRAY WINDOW PIXEL, INCREMENT BY ONE IN A COUNTING ARRAY, THE PIXELS ORTHOGONAL TO THE DIRECTION OF THE CORRESPONDING EDGE PIXEL
1200
FORM A COUNTER MAP BASED ON THE INCREMENTATION
1202
FIND THE MAXIMUM IN THE COUNTER MAP
1204
SPOT CENTER FINDING
PRUNE THE PIXELS IN THE EDGE DETECTION IMAGE BASED ON EACH PIXEL'S DIRECTIONAL OFFSET FROM THE IDENTIFIED CENTER
1206
FORM A RADIUS HISTOGRAM OF EDGE PIXEL'S BASED ON THEIR DISTANCE FROM THE IDENTIFIED CENTER
1208
IDENTIFY THE PEAK IN THE RADIUS HISTOGRAM
1210
RADIUS VALUE FOR THE PEAK IS THE RADIUS OF THE CIRCLE
1212
SPOT RADIUS FINDING (HOUGH TRANSFORM)

FIG. 12

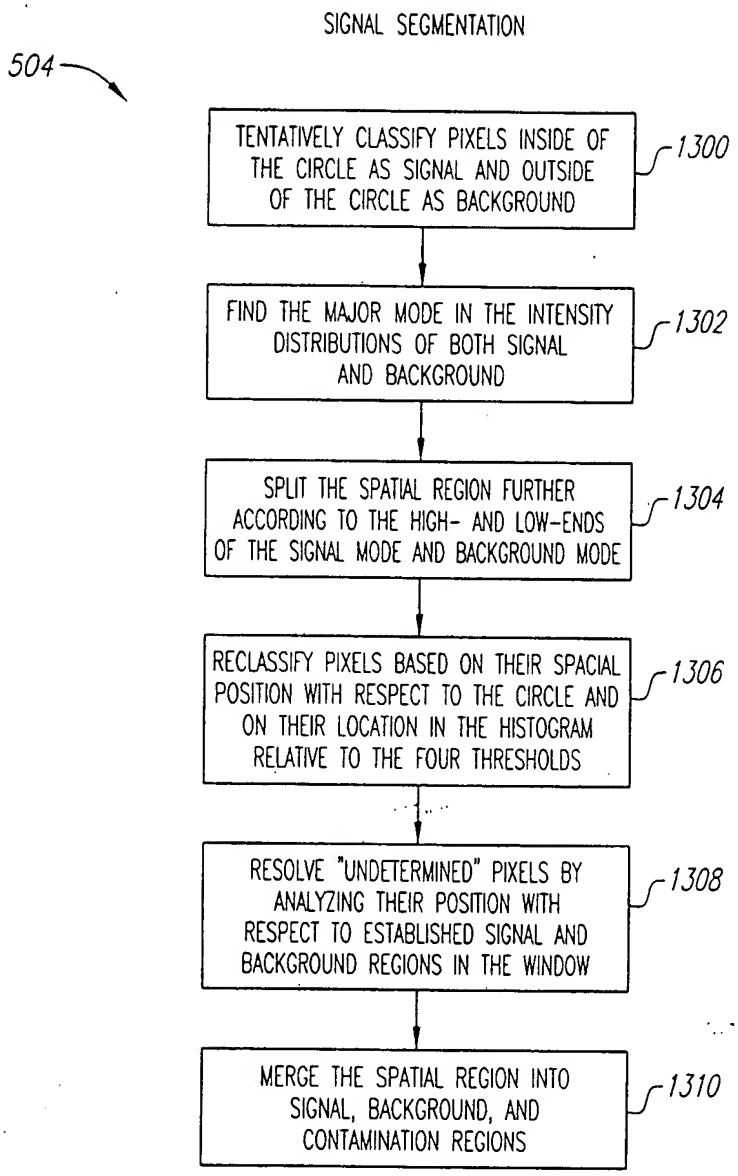
SIGNAL SEGMENTATION
504
TENTATIVELY CLASSIFY PIXELS INSIDE OF THE CIRCLE AS SIGNAL AND OUTSIDE OF THE CIRCLE AS BACKGROUND
1300
FIND THE MAJOR MODE IN THE INTENSITY DISTRIBUTIONS OF BOTH SIGNAL AND BACKGROUND
1302
SPLIT THE SPATIAL REGION FURTHER ACCORDING TO THE HIGH- AND LOW-ENDS OF THE SIGNAL MODE AND BACKGROUND MODE
1304
RECLASSIFY PIXELS BASED ON THEIR SPACIAL POSITION WITH RESPECT TO THE CIRCLE AND ON THEIR LOCATION IN THE HISTOGRAM RELATIVE TO THE FOUR THRESHOLDS
1306
RESOLVE "UNDETERMINED" PIXELS BY ANALYZING THEIR POSITION WITH RESPECT TO ESTABLISHED SIGNAL AND BACKGROUND REGIONS IN THE WINDOW
1308
MERGE THE SPATIAL REGION INTO SIGNAL, BACKGROUND, AND CONTAMINATION REGIONS
1310

FIG. 13

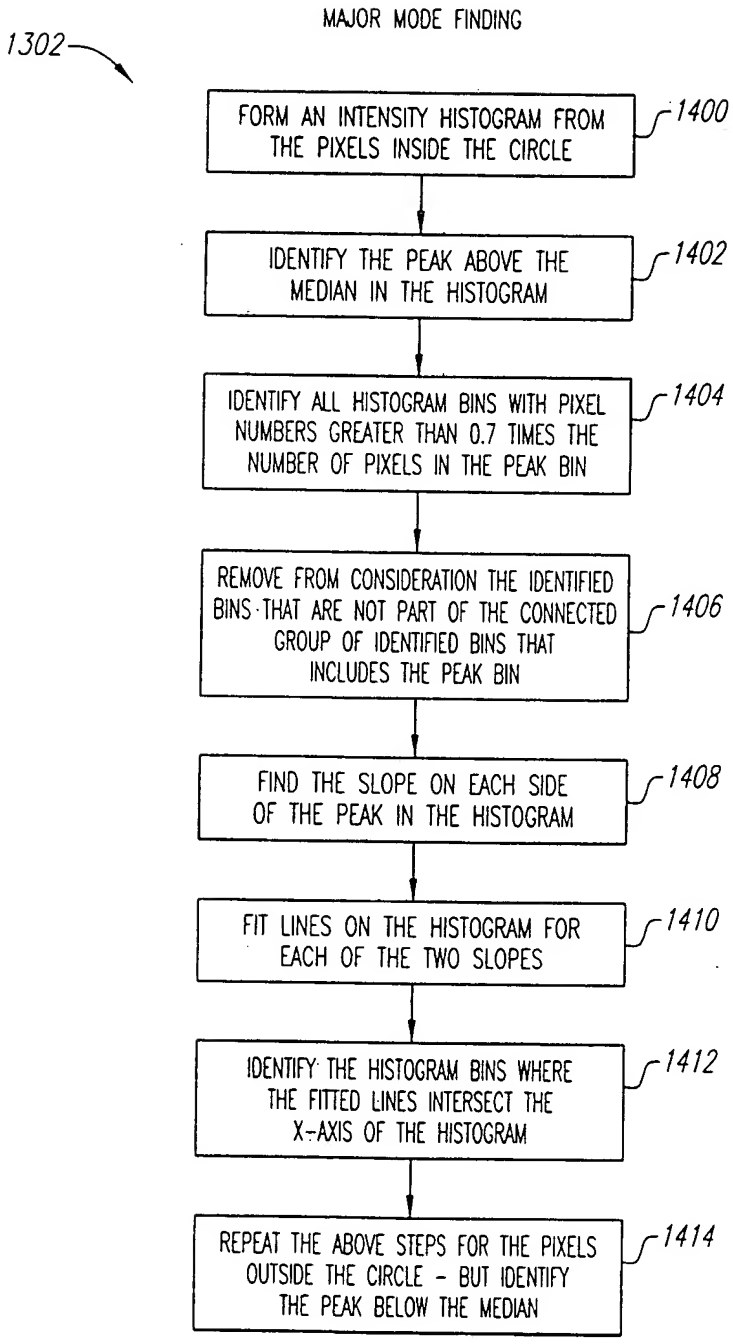
MAJOR MODE FINDING
1302
FORM AN INTENSITY HISTOGRAM FROM THE PIXELS INSIDE THE CIRCLE
1400
IDENTIFY THE PEAK ABOVE THE MEDIAN IN THE HISTOGRAM
1402
IDENTIFY ALL HISTOGRAM BINS WITH PIXEL NUMBERS GREATER THAN 0.7 TIMES THE NUMBER OF PIXELS IN THE PEAK BIN
1404
REMOVE FROM CONSIDERATION THE IDENTIFIED BINS THAT ARE NOT PART OF THE CONNECTED GROUP OF IDENTIFIED BINS THAT INCLUDES THE PEAK BIN
1406
FIND THE SLOPE ON EACH SIDE OF THE PEAK IN THE HISTOGRAM
1408
FIT LINES ON THE HISTOGRAM FOR EACH OF THE TWO SLOPES
1410
IDENTIFY THE HISTOGRAM BINS WHERE THE FITTED LINES INTERSECT THE X-AXIS OF THE HISTOGRAM
1412
REPEAT THE ABOVE STEPS FOR THE PIXELS OUTSIDE THE CIRCLE - BUT IDENTIFY THE PEAK BELOW THE MEDIAN
1414

FIG. 14

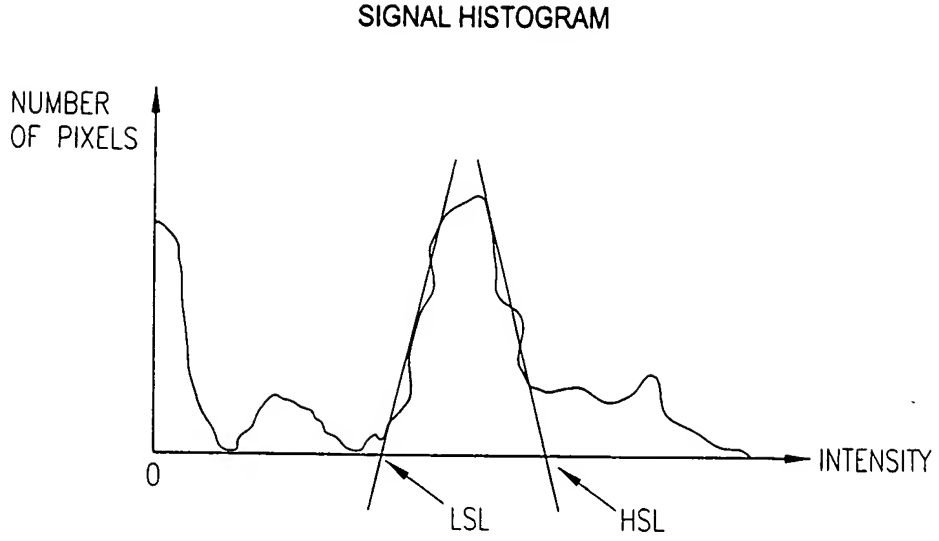

FIG. 15A

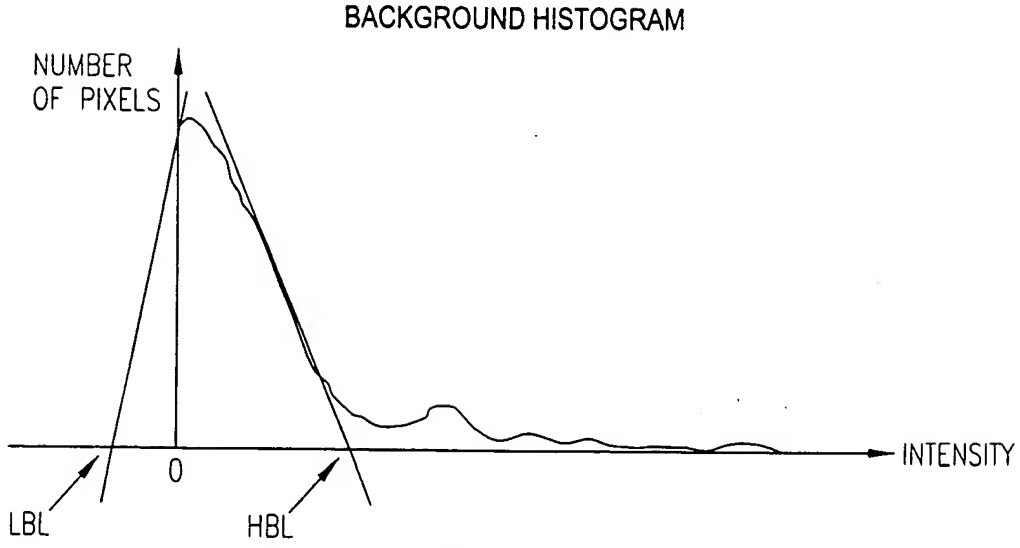

FIG. 15B

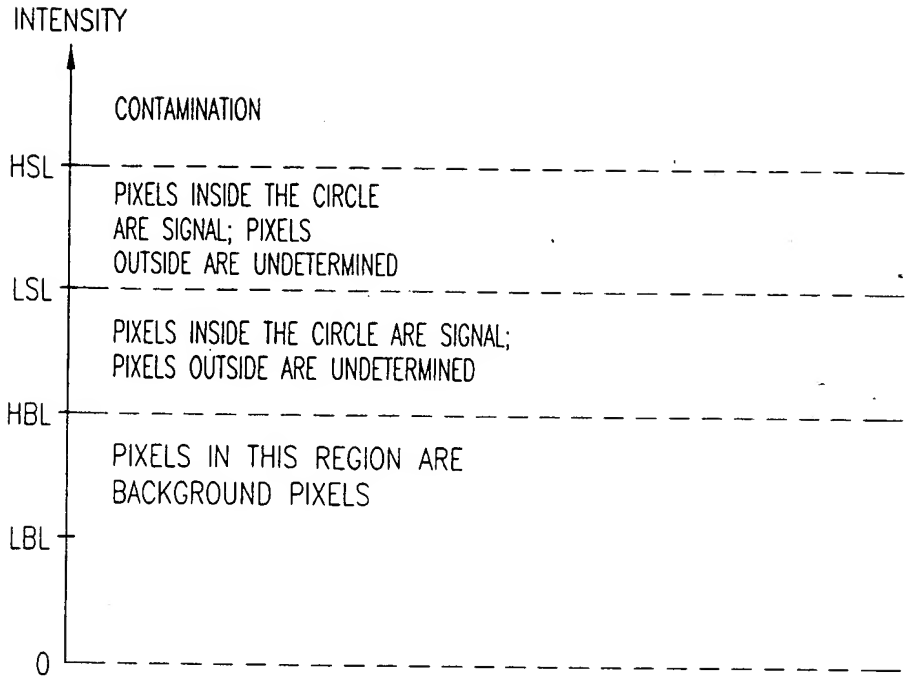

FIG. 16A

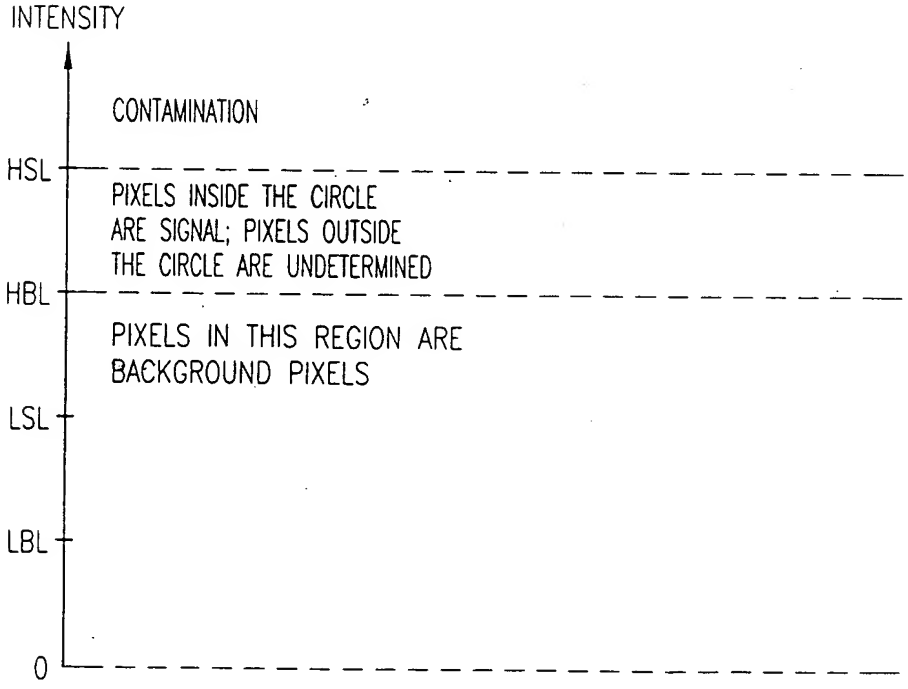

FIG. 16B

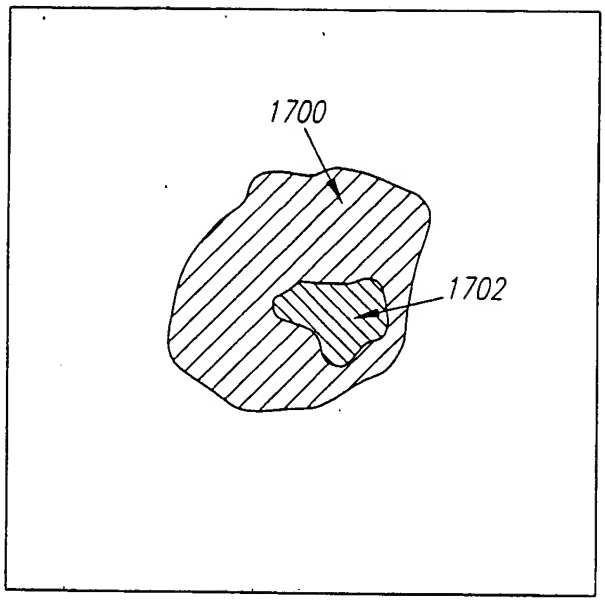

FIG. 17A

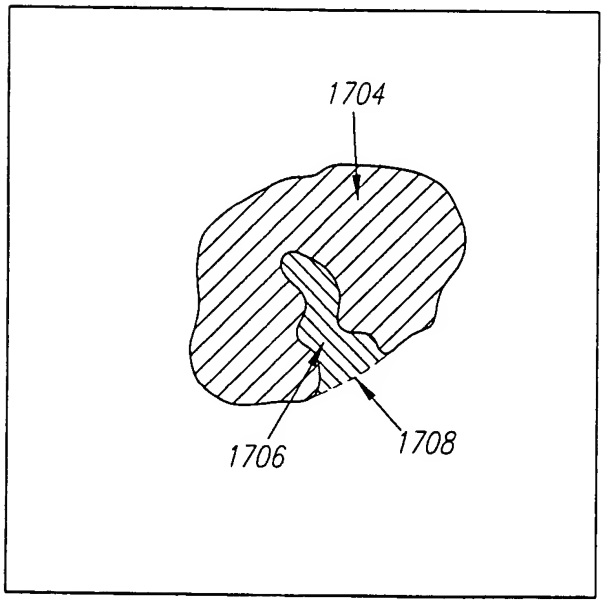

FIG. 17B